

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

OFFICE

**RECEIVED**

JAN 15 2003

TECH CENTER 1600/2900

**SMITTAL**

**Sir:**

375.00 0P

6. \_\_\_\_\_ The Commissioner is hereby authorized to charge the following fees, or credit any overpayment, to Deposit Account No. 03-3125.

\_\_\_\_\_ RCE fee required under 37 C.F.R. § 1.17(e).  
\_\_\_\_\_ Extension of time fee (37 C.F.R. §§ 1.136 and 1.17).  
\_\_\_\_\_ Other fees \_\_\_\_\_.

7. X Three copies of this sheet are enclosed.

Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Box RCE, Washington, D.C. 20231.

Alan J. Morrison  
Reg. No. 37,399

Date

1/2/03

John P. White  
Registration No. 28,678  
Alan J. Morrison  
Registration No. 37,399  
Attorneys for Applicants  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
(212) 278-0400

74. (Amended) A method for sequencing DNA which comprises:

- (a) treating the DNA with a mixture comprising an oligonucleotide primer, a DNA polymerase, four different deoxynucleotides, and four different labeled dideoxynucleotides, under conditions permitting a deoxynucleotide or a labeled dideoxynucleotide or both to be incorporated into a DNA sequencing fragment, wherein each different deoxynucleotide and each different labeled dideoxynucleotide is complementary to one of the four nucleotides present in the DNA, wherein each labeled dideoxynucleotide comprises a chemical moiety attached via a linker to the dideoxynucleotide; and wherein each of the four different labeled dideoxynucleotides has a molecular weight which can be distinguished from the molecular weight of the other three labeled dideoxynucleotides using mass spectrometry;
- (b) generating a plurality of DNA sequencing fragments having different lengths that are terminated with the labeled dideoxynucleotides so as to generate a plurality of different labeled DNA sequencing fragments, wherein each DNA sequencing fragment has a 3' end and the chemical moiety is attached via the linker to the 3' end of the DNA sequencing fragment;
- (c) contacting the labeled DNA sequencing fragments with a surface coated with a compound that specifically interacts with the chemical moiety attached via the linker to the 3' end of the DNA sequencing fragments, thereby capturing the labeled DNA sequencing fragments on the surface, wherein the contacting is performed in a system comprising (i) a channel whose surface is coated with a compound that specifically interacts

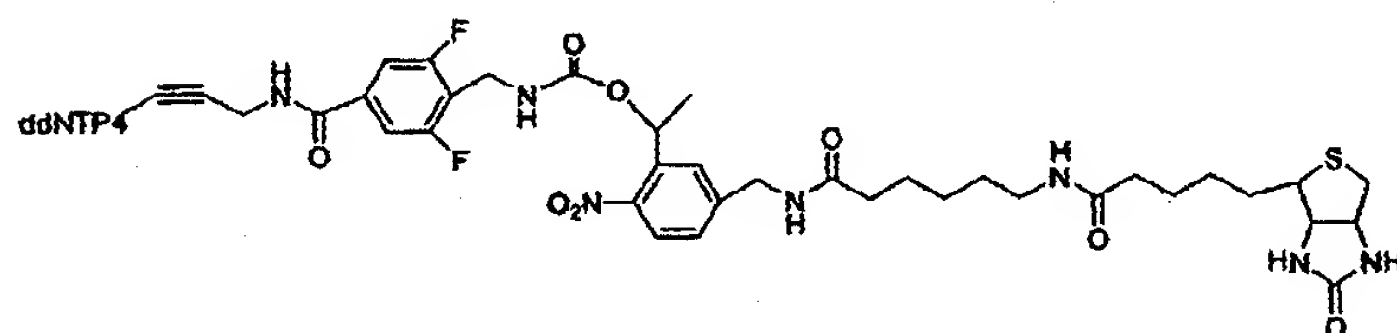
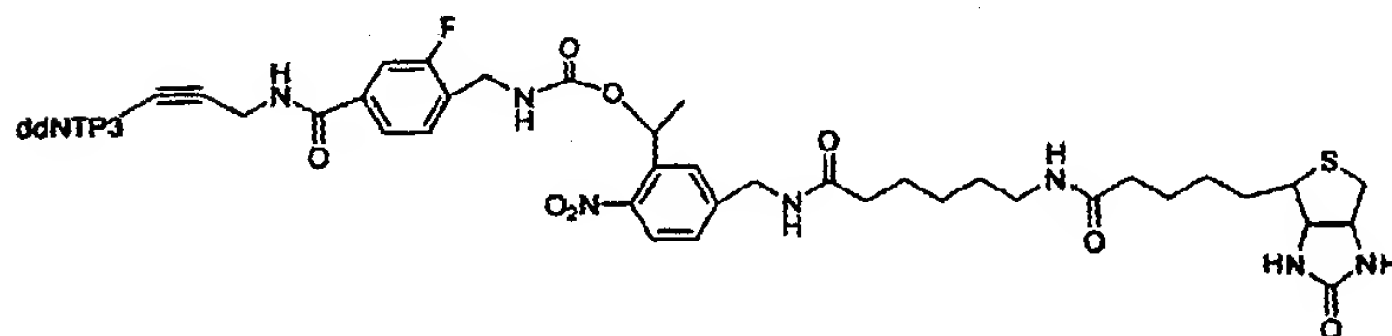
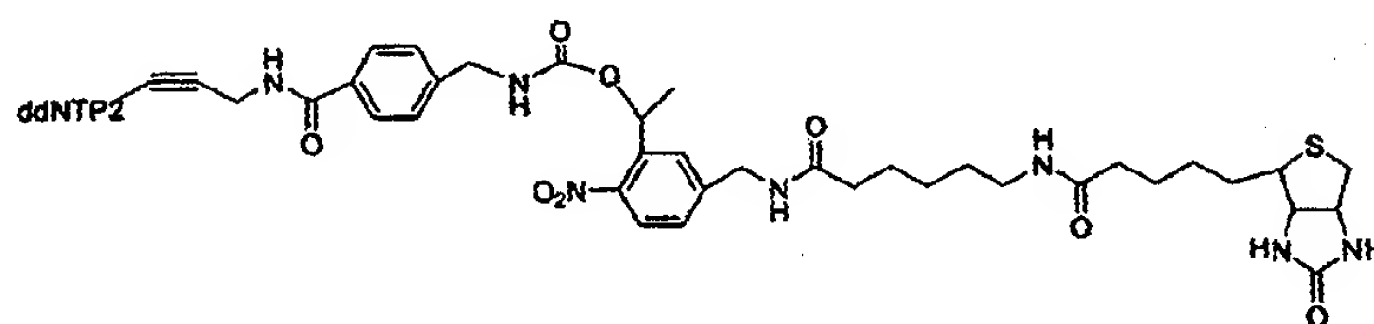
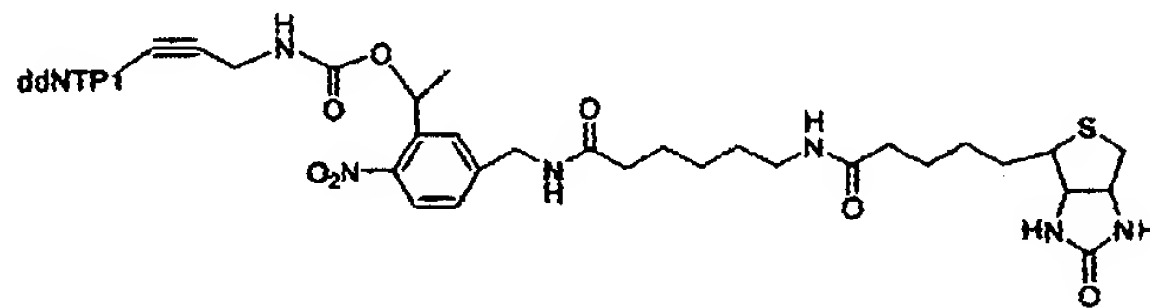
Applicants: Jingyue Ju et al.  
U.S. Serial No.: 09/823,181  
Filed March 30, 2001  
Page 3

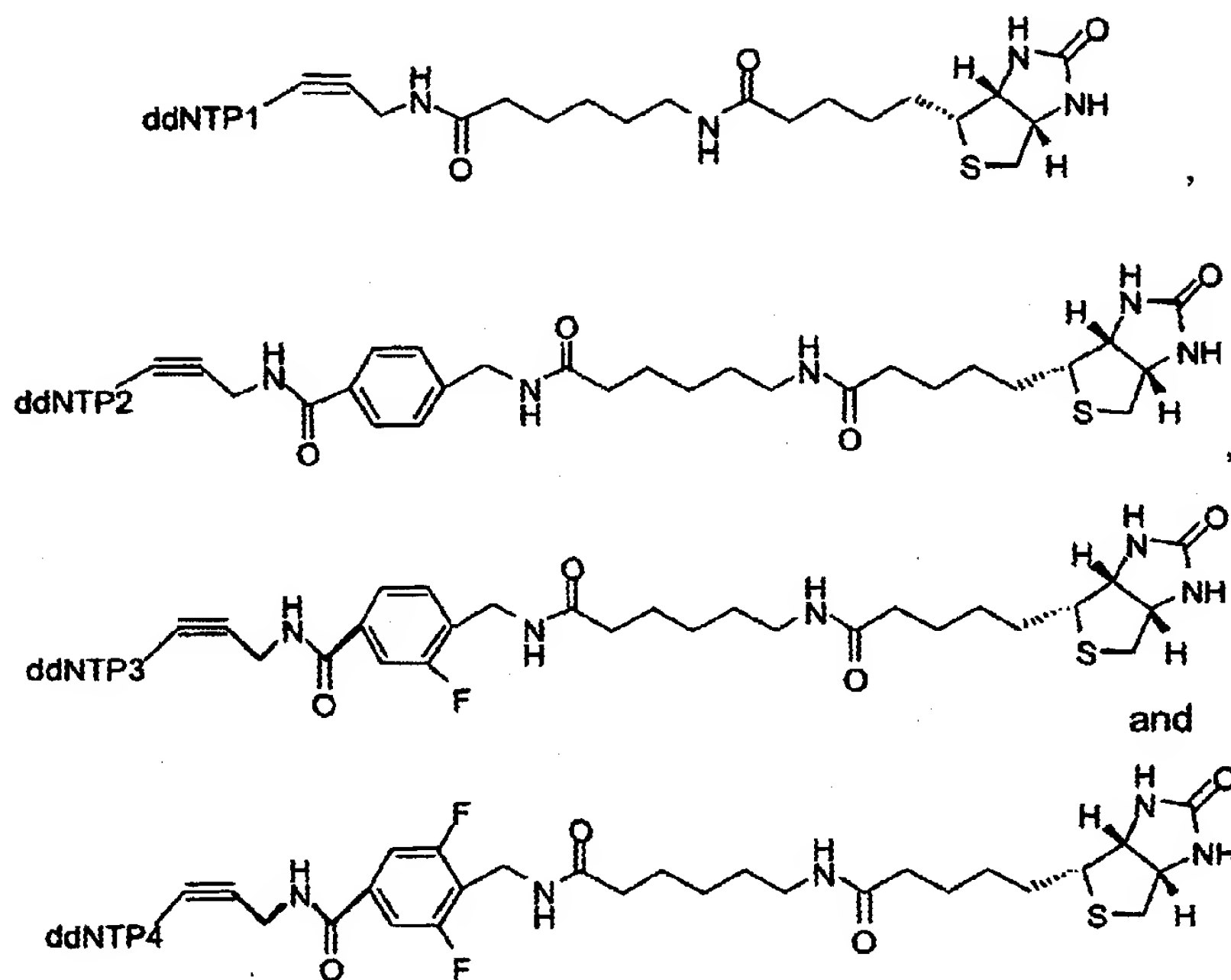
with the chemical moiety, wherein the channel comprises a plurality of ends, (ii) a plurality of wells each suitable for holding a sample, (iii) a connection between each end of the channel and a well, and (iv) a means for moving the sample through the channel between wells;

- (d) washing the surface to remove non-bound components;
- (e) treating the labeled DNA sequencing fragments so as to release the labeled DNA sequencing fragments from the surface; and
- (f) determining the difference in molecular weight between different labeled DNA sequencing fragments which are represented as adjacent peaks on a mass spectra of the labeled DNA sequencing fragments produced using mass spectrometry, so as to sequence the DNA;

wherein either (i) the labeled dideoxynucleotides are biotinylated dideoxynucleotides selected from the group consisting of

Applicants: Jingyue Ju et al.  
U.S. Serial No.: 09/823,181  
Filed March 30, 2001  
Page 4

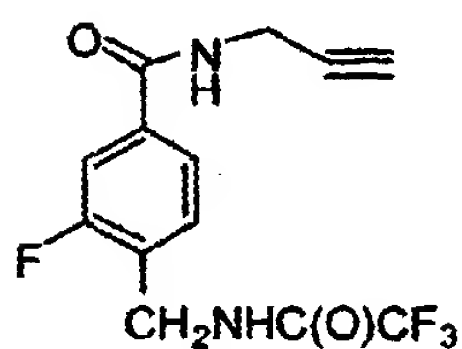
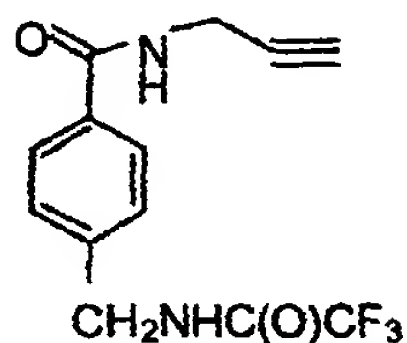




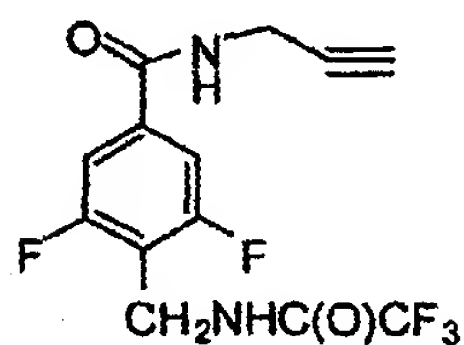
where ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides; or

Applicants: Jingyue Ju et al.  
U.S. Serial No.: 09/823,181  
Filed March 30, 2001  
Page 6

(ii) the linker is selected from the group consisting of



and



#### REMARKS

Claims 74-92 are presently pending and under examination. Applicants have herein amended claim 74 and maintain that these changes introduce no new matter into the application. Support for the amendment to claim 74 can be found in the specification as originally filed at, *inter alia*, page 32, lines 11-23.